Abstract No. Chan0088

Structural Studies on the Interaction of Two Cofactors, DNA and Peptide-pVIc, with Adeno Virus Protease (AVP) in Solution Using Synchrotron Protein Footprinting

S. Gupta (AECOM), M. Baniecki (State U. of NY at Stony Brook), W. Mangel (BNL), M. Chance (AECOM)

Beamline(s): X28C

Human Adeno Virus Protease (AVP) belongs to a subclass of cystein protease. AVP requires two cofactors for its maximal proteolysis activity, the 11 amino acid residue peptide pVIc and viral DNA. The fully active complex of enzyme and cofactor then moves along the viral DNA, cleaving other viral precursor protein to make the virus particle infectious. Structural details of this type of simulation of protease activity by binding to DNA molecule is not known yet. Synchrotron protein footprinting is used to identify the specific side chain residues on the protein surface that are involved in the binding of DNA molecule. Exposure of free AVP, AVP-pVIc binary complex, and in there complexes with 12 mer double stranded DNA to synchrotron X-ray generates stable oxidative modification of certain amino acid side chains in AVP. Extent and the site of modifications which are dependent on its intrinsic reactivity and solvent accessibility are determined by mass spectroscopic analysis. Comparison of DNA binding studies with the free AVP and AVP-pVIc binary complex also reveal the role of 11 amino acid residue peptide, pVIc in the conformational change of the protease to make it fully functional protease. These results will be used to construct a high resolution map of the solvent accessible reactive sites in AVP which will help to design drugs capable to bind and block these sites. This study can be used to develop a new form of antiviral therapy using multiple drugs against these three target sites - the active site, the cofactor binding site, and the DNA binding site on the same virus-coded protein.